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PHARMACOLOGICAL REVIEWS

Understanding the neural mechanisms of general anesthesia from interaction with sleep-wake state: a decade of discovery

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Supplementary Table 1. Effects of selective manipulation of the brain structures on inhaled anesthetic responses.

Structures	Neurons/ neural circuits	Anesthetics	Manipulation	Induction	Emergence	Reference
PFC	Glutamatergic terminals in the DMH	Isoflurane	Chemogenetic activation		RORR↓	(Zhong et al., 2017)
diLS	GABAergic neurons	Isoflurane	Optogenetic activation		EEG (Burst number↑ Burst duration↑ BSR↓); EMG (-); RORR↓	(Wang et al., 2021a)
		Isoflurane	Optogenetic inhibition		EEG (-); EMG (-); RORR↑	
NAc	D1R neurons	Sevoflurane	Chemogenetic activation	EC50-LORR↑; LORR↑	RORR↓	(Bao et al., 2021)
		Sevoflurane	Chemogenetic inhibition	EC50-LORR↓; LORR↓	RORR↑	
		Sevoflurane	Optogenetic activation		EEG (BSR↓ delta↓ beta↑); EMG↑; Arousal score↑	
BF	Cholinergic neurons	Isoflurane	Gene knockout	EC50-LORR↓	Hippocampal high-gamma power↓	(Leung et al., 2021)
		Isoflurane	Genetic lesions	LORR↓	EEG (delta↑ beta↓); RORR↑	(Luo et al., 2020)
		Isoflurane	Chemogenetic activation	LORR↑	EEG (delta↓ beta↑); RORR↓	
		Isoflurane	Optogenetic activation	LORR↑	RORR↓	
	GABAergic SOM-expressing neurons	Isoflurane	Genetic lesions	LORR↓	EEG (delta↓); RORR↑	(Cai et al., 2021)
	GABAergic PV-expressing neurons	Isoflurane	Genetic lesions	LORR↓	EEG (-); RORR (-)	
	GABAergic SOM-expressing neurons	Isoflurane	Chemogenetic activation	LORR↓	EEG (delta↑ gamma↓); RORR↑	

	GABAergic PV-expressing neurons	Isoflurane	Chemogenetic activation	LORR↑	EEG (delta↓); RORR (-)	
	GABAergic SOM-expressing neurons	Isoflurane	Chemogenetic inhibition	LORR↑	EEG (delta↓); RORR↓	
	GABAergic PV-expressing neurons	Isoflurane	Chemogenetic inhibition	LORR (-)	EEG (delta↑); RORR (-)	
PVT	Glutamatergic neurons	Isoflurane	Optogenetic activation		EEG (BSR↓ Burst duration↑ delta↑ theta↓); EMG (-); RORR↓	(Ren et al., 2018)
		Sevoflurane	Chemogenetic inhibition	EEG (delta↑); EC50-LORR↓; LORR↓	EEG (delta↑ theta↓); EC50-RORR↓; RORR↑	(Li et al., 2022)
	Sevoflurane	Optogenetic activation	LORR↑	EEG (BSR↓ delta↑ alpha↑ beta↑ gamma↑); Arousal score↑; RORR↓		
	Glutamatergic terminals in the BNST	Sevoflurane	Optogenetic activation	LORR↑	EEG (BSR↓ delta↑); Arousal score↑; RORR↓	
VMT	Matrix cells	Sevoflurane+ Dexmedetomidine	Optogenetic activation		EEG (slow wave activity↓ theta↓ gamma↑); Whisker EMG↑; Behavioral Arousal↑	(Honjoh et al., 2018)
SON and para-SON	AANs	Isoflurane	Optogenetic activation	Induction time (-)	Fully awake↑; Duration of unconsciousness↑	(Jiang-Xie et al., 2019)
		Isoflurane	Optogenetic inhibition	Induction time (-)	Fully awake↓; Duration of unconsciousness↓	
POA	TAC1 neurons	Isoflurane	Chemogenetic activation	EC50-LORR↑	EC50-RORR↑	(Reitz et al., 2020)
		Isoflurane	Chemogenetic inhibition	EC50-LORR (-)	EC50-RORR (-)	
		Sevoflurane	Chemogenetic activation	EC50-LORR (-)	EC50-RORR↑	
		Sevoflurane	Chemogenetic inhibition	EC50-LORR (-)	EC50-RORR (-)	

POA (VLPO)	Galaninergic neurons	Isoflurane	Galanin-saporin lesions 6 day	EC50-LORR↑		(Moore et al., 2012)
		Isoflurane	Galanin-saporin lesions 24 day	EC50-LORR↓		
	GABAergic neurons	Isoflurane	Chemogenetic activation	LORR (-)	RORR (-)	(Vanini et al., 2020)
	Glutamatergic neurons	Isoflurane	Chemogenetic activation	LORR (-)	LORR (-)	
POA (MnPO)	GABAergic neurons	Isoflurane	Chemogenetic activation	LORR (-)	RORR (-)	
	Glutamatergic neurons	Isoflurane	Chemogenetic activation	LORR (-)	0.5 mg/kg CNO: RORR (↑) 1.0 mg/kg CNO: RORR (-)	
LH	GABAergic terminals in the TRN	Isoflurane	Optogenetic activation		EEG (Burst duration↑ BSR↓); EMG↑	(Herrera et al., 2016)
	Glutamatergic neurons	Isoflurane	Genetic lesions	LORR↓	RORR↑	(Zhao et al., 2021a)
		Isoflurane	Chemogenetic activation	LORR↑	RORR↓	
		Isoflurane	Chemogenetic inhibition	LORR↓	RORR↑	
		Isoflurane	Optogenetic activation		EEG (BSR↓ delta↓ alpha↑ beta↑ gamma↑)	
		Isoflurane	Optogenetic inhibition		EEG (BSR (-) beta↓)	
	Glutamatergic terminals in the LHb	Isoflurane	Optogenetic activation	LORR↑	EEG (BSR↓ delta↓ beta↑ gamma↑); RORR↓	
		Isoflurane	Optogenetic inhibition	LORR↓	EEG (BSR (-) delta↑ beta↓ gamma↓); RORR↑	
LH (Pef)	Orexinergic neurons	Isoflurane	Chemogenetic activation		EEG (delta↓ alpha↑ beta↑); EMG↑; RORR↓	
		Isoflurane	Optogenetic activation	LORR (-)	EEG(BSR↓); RORR↓	(Wang et al., 2020)
		Isoflurane	Chemogenetic activation	EC50-LORR (-); LORR (-)	EC50-RORR↑; RORR↓	(Zhao et al., 2021b)

		Isoflurane	Chemogenetic inhibition	EC50-LORR↓; LORR (-)	EC50-RORR↓; RORR↑		
		Desflurane	Chemogenetic activation	EC50-LORR↑; LORR↑	EC50-RORR↑; RORR↓		
		Desflurane	Chemogenetic inhibition	EC50-LORR↓; LORR↓	EC50-RORR↓; RORR↑		
		Isoflurane	Optogenetic activation		EEG(BSR↓)		
		Desflurane	Optogenetic activation		EEG (BSR↓ delta↓ alpha↑ beta↑ gamma↑)		
	Orexiner- gic terminals in the PVT	Isoflurane	Chemogenetic activation	LORR (-)	RORR↓		
		Isoflurane	Chemogenetic inhibition	LORR (-)	RORR↑		
		Desflurane	Chemogenetic activation	LORR↑	RORR↓		
		Desflurane	Chemogenetic inhibition	LORR↓	RORR↑		
		Isoflurane	Optogenetic activation		EEG (BSR↓)		
		Desflurane	Optogenetic activation		EEG (BSR↓)		
	Orexiner- gic terminals in the BF	Isoflurane	Optogenetic activation		EEG (BSR↓ delta↓ theta↑ beta↑ gamma↑); Arousal score↑; RORR↓		(Wang et al., 2020)
	Orexiner- gic terminals in the LC	Isoflurane	Optogenetic activation		EEG (BSR↓ delta↓ beta↑ gamma↑); Arousal score↑; RORR↓		

	Orexinergic terminals in the VTA	Isoflurane	Optogenetic activation		EEG (BSR↓ delta↓ alpha↑ beta↑ gamma↑); Arousal score↑; RORR↓	(Li et al., 2019)
		Isoflurane	Optogenetic inhibition		EEG (BSR (-) theta↓ beta↓); Arousal score (-); RORR↑	
DMH	Glutamatergic terminals at LH (Pef)	Isoflurane	Chemogenetic activation		RORR↓	(Zhong et al., 2017)
LHb	Glutamatergic neurons	Isoflurane	Genetic lesions	LORR↑	EEG (Maintenance: delta↓ alpha↑ beta↑ BSR↓; Recovery: delta↓); RORR↓	(Liu et al., 2021a)
		Isoflurane	Chemogenetic activation	LORR↓	EEG (delta↑ gamma↓ BSR↑); RORR↑	
		Isoflurane	Chemogenetic inhibition	LORR↑	EEG (delta↓ theta↑ beta↑ BSR↓); RORR↓	
	Isoflurane	Optogenetic activation	EEG (delta↑ beta↓ gamma↓); LORR↓	EEG (delta↑ gamma↓); RORR↑		
	Glutamatergic terminals in the RMTg	Isoflurane	Optogenetic activation	EEG (delta↑ alpha↓ beta↓ gamma↓); LORR↓	EEG (delta↑ beta↓ gamma↓); RORR↑	
	Glutamatergic terminals in the VTA	Isoflurane	Optogenetic activation	LORR (-)	RORR (-)	
VTA	Dopaminergic neurons	Isoflurane	Lesions (infusion of 6-hydroxydopamine)	EC50-LORR (-); LORR (-)	RORR (-)	(Zhou et al., 2015)
		Isoflurane	Optogenetic activation		EEG (power < 5 Hz ↓ 6-17 Hz ↓); Arousal score↑	(Taylor et al., 2016)
		Sevoflurane	Chemogenetic activation	EEG (delta↓ beta↑); LORR↑	EEG (delta↓ theta↑ alpha↓ beta↑ gamma↑); RORR↓	(Song et al., 2021)
		Sevoflurane	Optogenetic activation	EEG (delta↓ beta↑ gamma↑); LORR↑	EEG (theta↓ beta↑ gamma↑); RORR↓	(Gui et al., 2021)
	Dopaminergic terminals in the	Sevoflurane	Optogenetic activation	EEG (delta↓ gamma↑); LORR↑	EEG (delta↓ gamma↑); RORR↓	

	NAc	Sevoflurane	Optogenetic inhibition	EEG (theta↑ alpha↑ gamma↓); LORR↓	EEG (delta↑ alpha↓ beta↓ gamma↓); RORR↑	
	Dopaminergic terminals in the PrL	Sevoflurane	Chemogenetic activation (retrograde label)	EEG (delta↓ theta↓ beta↑ gamma↑); LORR↑	EEG (delta↓ alpha↓ beta↑ gamma↑); RORR↓	(Song et al., 2021)
		Sevoflurane	Chemogenetic activation (anterograde label)	EEG (delta↓ gamma↑); LORR↑	EEG (alpha↓ gamma↑); RORR↓	
		Sevoflurane	Optogenetic activation	EEG (delta↓ alpha↓ gamma↑); LORR↑	EEG (delta↓ beta↑ gamma↑); RORR↓	
	GABAergic neurons	Isoflurane	Optogenetic activation		EEG (BSR↑ delta↑ beta↓ gamma↓)	(Yin et al., 2019)
		Isoflurane	Optogenetic inhibition		EEG (BSR↓ delta↓ theta↓ alpha↓ gamma↑)	
		Isoflurane	Chemogenetic activation	EC50-LORR↓; LORR↓	EC50-RORR↓; RORR↑	
		Isoflurane	Chemogenetic inhibition	EC50-LORR↑; LORR↑	EC50-RORR↑; RORR↓	
	GABAergic terminals in the LH	Isoflurane	Optogenetic activation	LORR↓	EEG (BSR↑ delta↑ gamma↓); RORR↑	
		Isoflurane	Optogenetic inhibition	LORR↑	EEG (BSR↓ delta ↓ alpha↓ gamma↑); RORR (-)	
RMTg	GABAergic neurons	Sevoflurane	Chemogenetic activation	EC50-LORR↓		(Vlasov et al., 2021)
vPAG	Dopaminergic neurons	Isoflurane	Lesions (infusion of 6-hydroxydopamine)	LORR↓	EEG (Maintenance: delta↑; Recovery: (-)); RORR↑	(Liu et al., 2020b)
DRN	Serotonergic neurons	Isoflurane	Optogenetic activation		EEG (BSR↓)	(Li et al., 2021)
		Isoflurane	Optogenetic inhibition		EEG (BSR↑)	
		Isoflurane	Chemogenetic activation	LORR (-)	RORR↓	
		Isoflurane	Chemogenetic inhibition	LORR (-)	RORR↑	

LC	Noradrenergic neurons	Isoflurane	Chemogenetic activation	LORR↑	EEG (BSR↓ delta↓ theta↑); RORR↓	(Vazey and Aston-Jones, 2014)
		Isoflurane	Chemogenetic activation	LORR (-)	EEG (BSR (-) delta↓ alpha↑); RORR↓	(Ao et al., 2021b)
	Noradrenergic terminals in the PVT	Isoflurane	Chemogenetic inhibition	LORR (-)	RORR↑	
		Isoflurane	Optogenetic activation	LORR (-)	EEG (BSR↓ delta↓ theta↑ alpha↑); RORR↓	
PB	Glutamatergic neurons	Sevoflurane	Chemogenetic activation	EC50-LORR↑; LORR↑	RORR↓	(Wang et al., 2019)
		Sevoflurane	Chemogenetic inhibition	EC50-LORR↓; LORR (-)	RORR↑	
		Sevoflurane	Optogenetic activation		EEG (delta↓ theta↑)	

↑↓ represent different indicators that increased or decreased compared to the control group, respectively; (-) represents no significant difference compared to the control group.

Supplementary Table 2. Effects of unselective manipulation of the brain structures on inhaled anesthetic responses.

Structure	Anesthetics	Subject	Manipulation	Induction	Emergence	Reference
PFC→DMH projection	Isoflurane	Rats	Chemogenetic activation		RORR↓	(Zhong et al., 2017)
PFC (PrL)	Sevoflurane	Rats	Dopamine receptor agonist	LORR↑	RORR↓	(Song et al., 2021)
	Sevoflurane	Rats	Dopamine receptor antagonist	LORR↓	RORR↑	
	Sevoflurane	Rats	Cholinergic agonist		EEG (theta/delta↑); wake-like behavior↑	(Pal et al., 2018)
	Sevoflurane	Rats	NE		EEG (theta/delta↑); wake-like behavior (-)	
Posterior parietal cortex	Sevoflurane	Rats	Cholinergic agonist		EEG (theta/delta↑); wake-like behavior (-)	
	Sevoflurane		NE		EEG (theta/delta↑); wake-like behavior (-)	
Medial parietal association cortex	Sevoflurane	Rats	Cholinergic agonist		EEG (theta/delta↑); wake-like behavior (-)	
CI	Isoflurane	Rats	Electrical stimulation		EEG(BSR↑)	(Pavel et al., 2019)
BF	Isoflurane	Rats	Orexin-A	LORR (-)	RORR↓	(Zhang et al., 2016)
	Isoflurane		Orexin-B	LORR (-)	RORR (-)	
	Isoflurane		Orexin-1 receptor antagonist	LORR (-)	RORR↑	
	Isoflurane		Orexin-2 receptor antagonist	LORR (-)	RORR (-)	
	Sevoflurane		Orexin-A	LORR (-)	EEG (30 or 100 pmol orexin-A: BSR↓); RORR↓	(Dong et al., 2009)
	Sevoflurane		Orexin-B	LORR (-)	EEG (30 pmol orexin-B: BSR (-), 100 pmol orexin-B: BSR (↓)); RORR (-)	
	Sevoflurane		Orexin-1 receptor antagonist	LORR (-)	RORR↑	

BF (nucleus basalis of Meynert)	Desflurane	Rats	NE		EEG (delta↓); Behavioral score↑	(Pillay et al., 2011)
BF (nucleus basalis magnocellularis)	Isoflurane	Rats	Histamine		EEG(BSR↓ delta↑ theta↑); RORR↓	(Luo and Leung, 2009)
	Isoflurane	Rats	Histamine receptor 1 antagonist		RORR↑	
	Isoflurane	Rats	Histamine receptor 2 antagonist		RORR (-)	
MS	Isoflurane	Rats	Electrolytic lesions	EC50-LORR↓	RORR↑	(Leung et al., 2013)
	Halothane	Rats	Electrolytic lesions		RORR↑	
CLT	Isoflurane	Monkeys	Electrical stimulation		Arousal score↑	(Redinbaugh et al., 2020)
PVT	Isoflurane	Mice	D2R agonist infusion	LORR (-)	EEG(BSR↓); RORR↓	(Ao et al., 2021a)
	Isoflurane		D2R antagonist infusion	LORR (-)	EEG (BSR (-)); RORR↑	
	Isoflurane	Rats	Orexin-A	LORR (-)	RORR↓	(Zhao et al., 2021b)
	Isoflurane	Rats	Orexin-B	LORR (-)	RORR↓	
	Desflurane	Rats	Orexin-A	LORR↑	RORR↓	
	Desflurane	Rats	Orexin-B	LORR↑	RORR↓	
	Isoflurane	Rats	Orexin-1 receptor antagonist	LORR (-)	RORR (-)	
	Isoflurane	Rats	Orexin-2 receptor antagonist	LORR (-)	RORR↑	
	Desflurane	Rats	Orexin-1 receptor antagonist	LORR (-)	RORR (-)	
	Desflurane	Rats	Orexin-2 receptor antagonist	LORR↓	RORR↑	
PVT-BNST projection	Sevoflurane	Mice	Chemogenetic inhibition	EC50-LORR↓; EEG (delta↑); LORR↓	EC50 (RORR)↓; EEG (delta↑); RORR↑	(Li et al., 2022)
POA(VLPO)	Isoflurane	Rats	Orexin-saporin lesions	LORR (-)	EEG (BSR↑); RORR↑	(Eikermann et al., 2011)
DMH-LH(Pef) projection	Isoflurane	Rats	Chemogenetic activation		RORR↓	(Zhong et al., 2017)

DMH- POA(VLPO) projection	Isoflurane	Rats	Chemogenetic activation		RORR↓	
TMN	Isoflurane	Rats	Orexin-saporin lesions	EC50-LORR↓; LORR (-)	RORR↑	(Luo and Leung, 2011)
VTA	Isoflurane	Rats	Orexin-A	LORR (-)	EEG (BSR↓); RORR↓	(Li et al., 2019)
	Isoflurane		Orexin-B	LORR (-)	EEG (-); RORR (-)	
	Isoflurane		Orexin-1 receptor antagonist	LORR (-)	EEG (-); RORR↑	
	Isoflurane		Orexin-2 receptor antagonist	LORR (-)	EEG (-); RORR (-)	
VTA-NAc	Sevoflurane	Mice	Chemogenetic activation	EEG (delta↓gamma↑); LORR↑	EEG (delta↓ gamma↑); RORR↓	(Gui et al., 2021)
	Sevoflurane	Mice	Chemogenetic inhibition	EEG (delta↑ beta↓ gamma↓); LORR↓	EEG (delta↑ alpha↓ beta↓ gamma↓); RORR↑	
DRN	Isoflurane	Rats	Orexin-A	LORR (-)	EEG(BSR↓delta↓); RORR↓	(Yang et al., 2019)
	Isoflurane		Orexin-B	LORR (-)	EEG (BSR (-)); RORR (-)	
	Isoflurane		Orexin-1 receptor antagonist	LORR (-)	RORR↑	
	Isoflurane		Orexin-2 receptor antagonist	LORR (-)	RORR (-)	
vPAG	Isoflurane	Rats	GABA _A receptor agonist	LORR↓	EEG (delta↑ beta↓); RORR↑	(Liu et al., 2020b)
	Isoflurane		GABA _A receptor antagonist	LORR↑	EEG (delta↓); RORR↓	
LC	Isoflurane	Rats	GABA _B receptor antagonist		EEG (delta↓ theta↑); Behavioral emergence↑	(Hung et al., 2020)
PB	Isoflurane	Rats	Chemogenetic activation	LORR (-)	EEG (Maintenance: (-); Recovery: delta↓); RORR↓	(Luo et al., 2018)
medial PB	Sevoflurane	Mice	GABA _A receptor antagonist	1.5% sevoflurane: LORR↑; 3.0% sevoflurane: LORR (-)	1.5% sevoflurane: RORR↓; 3.0% sevoflurane: RORR (-)	(Xu et al., 2020)

↑↓ represent different indicators that increased or decreased compared to the control group, respectively; (-) represents no significant difference compared to the control group.

Supplementary Table 3. Effects of selective manipulation of the brain structures on intravenous anesthetic responses.

Structures	Neurons/ Neural circuits	Anesthetics	Manipulation	Induction	Emergence	Reference
BF	GABAergic SOM- expressing neurons	Propofol	Genetic lesions		LORR Durations↑; EEG (delta↓ beta↑)	(Cai et al., 2021)
		Propofol	Chemogenetic activation		LORR Durations↑; EEG (delta↑)	
		Propofol	Chemogenetic inhibition		LORR Durations↓; EEG (delta↓)	
	GABAergic PV- expressing neurons	Propofol	Genetic lesions		LORR Durations↑; EEG (-)	
		Propofol	Chemogenetic activation		LORR Durations (-); EEG (-)	
		Propofol	Chemogenetic inhibition		LORR Durations (-); EEG (delta↑ theta ↓)	
	Cholinergic neurons	Propofol	Genetic lesions		LORR Durations↑; EEG (delta↑ beta↓)	(Luo et al., 2020)
		Propofol	Chemogenetic activation		LORR Durations↓; EEG (delta↓ beta↑ gamma↑)	
		Propofol	Optogenetic activation		LORR Durations↓	
		Propofol	Optogenetic activation	LORR↑; ED50- LORR↑	RORR↓; medial PFC LFP (delta↓ beta↑ low gamma↑)	(Wang et al., 2021b)
Ketamine		Gene knockout	ED50-LORR↓		(Leung et al., 2021)	
Glutamatergic	Propofol	Optogenetic activation	LORR↑; ED50- LORR↑	RORR↓; medial PFC LFP (all band↑)	(Wang et al., 2021b)	
TRN	GABAergic neurons	Propofol	Chemogenetic activation	LORR (-)	RORR↓	(Liu et al., 2021b)
		Propofol	Chemogenetic inhibition	LORR (-)	RORR↑	
		Propofol	Optogenetic activation	LORR (-)	RORR↓	
		Propofol	Optogenetic inhibition	LORR (-)	RORR↑	
LHb	Glutamatergic	Propofol	Genetic lesions	ED50-LORR↑	LORR Durations↓; EEG (delta↓)	(Gelegen et al., 2018)

SN	Dopaminergic	Propofol	Lesions (infusion of 6-hydroxydopamine)	LORR (-); ED50-LORR (-)	RORR↑; EEG (delta↑)	(Fu Shi, 2017)
VTA	Dopaminergic	Propofol	Lesions (infusion of 6-hydroxydopamine)	LORR (-); ED50-LORR (-)	RORR↑	(Zhou et al., 2015)
		Ketamine		LORR (-); ED50-LORR (-)	RORR (-)	
LC	Noradrenergic terminals in the TRN	Propofol	Chemogenetic activation	ED50-LORR↓	RORR↑; EEG (delta↑)	(Zhang et al., 2019)
PB	Glutamatergic	Ketamine	Chemogenetic activation		RORR (-)	(Melonakos et al., 2021)

↑↓ represent different indicators that increased or decreased compared to the control group, respectively; (-) represents no significant difference compared to the control group.

Supplementary Table 4. Effects of unselective manipulation of the brain structures on intravenous anesthetic responses.

Structures	Anesthetics	Subject	Manipulation	Induction	Emergence	Reference
medial PFC	Propofol	Rats	GABA _A receptor antagonist	LORR↑	RORR↓	(Wang et al., 2016)
BF	Propofol	Rats	Ibotenic acid lesions	LORR (-)	RORR↑; EEG (delta↑)	(Liu et al., 2020a)
	Propofol		GABA _A receptor agonist	LORR (-)	RORR↑; EEG (delta↑ gamma↓)	
	Propofol		GABA _A receptor antagonist	LORR (-)	RORR↓; EEG (delta↓ gamma↑)	
	Propofol	Rats	Orexin-A	LORR (-)	RORR↓; EEG (BSR↓)	(Zhang et al., 2012)
	Propofol		Orexin-1 receptor antagonist	LORR (-)	RORR↑	
BF (NB)	Propofol	Rats	Ibotenic acid lesions	LORR (-)	RORR↑; EEG (delta↑)	(Xing et al., 2020)
	Propofol		GABA _A receptor agonist	LORR (-)	RORR↑; EEG (delta↑ gamma↓)	
	Propofol		GABA _A receptor antagonist	LORR (-)	RORR↓; EEG (delta↓)	
MS	Propofol	Rats	Electrolytic lesions	ED50-LORR↓	LORR Durations↑; Duration of loss of tail-pinch response ↑	(Leung et al., 2013)
CLT	Propofol	Monkeys	Electrical stimulation		Arousal score↑	(Redinbaugh et al., 2020)
CMT	Propofol	Rats	NE	LORR (-); ED50-LORR (-)	RORR↓; EEG (PFC: theta↑, anterior cingulate cortex: delta↓ theta↑ alpha↑)	(Fu et al., 2017)
TRN	Propofol	Mice	NE	LORR (-); ED50-LORR↓	RORR↑; EEG (delta↑)	(Zhang et al., 2019)
TMN	Ketamine	Rats	Orexin-saporin lesions	LORR (-); ED50-LORR (-)	RORR (-)	(Luo and Leung, 2011)

			Orexin-saporin lesions	LORR (-); ED50-LORR (-)	RORR (-)	
	Propofol		Histamine receptor 3 inverse agonist		RORR↓	(Xia et al., 2021)
			GABA		RORR↑	
				GABA _A receptor antagonist		LORR Durations↓
VLPO	Propofol	Rats	Ibotenic acid lesions	LORR↑	LORR Durations↓	(Zhang et al., 2015)
			GABA _A agonist	LORR↓	RORR↑	(Yuan et al., 2017)
			GABA _A antagonist	LORR↑	RORR↓	
vIPAG	Ketamine	Rats	Ibotenic acid lesions		Tail-flick latencies↓	(Lu et al., 2008)
LC	Propofol	Zebrafish	Two-photon laser lesions	LORR↓	RORR↑	(Du et al., 2018)
			Impair NE synthesis	LORR↓	RORR↑	
		Rats	GABA _A receptor antagonist	LORR (-)		(Zhang et al., 2015)
MPTA	Propofol	Rats	Ibotenic acid lesions	ED50-arousal score↑	RORR↑	(Minert et al., 2020)
	Ketamine			ED50-arousal score (-)	RORR (-)	
PB	Propofol	Rats	Chemogenetic activation	LORR (-)	RORR↓; EEG (Maintenance: (-), recovery: delta↓ beta↑)	(Luo et al., 2018)
PnO			GABA synthesis inhibitor	LORR↓	RORR (-)	(Vanini et al., 2014)
	Propofol		GABA uptake inhibitor	LORR↑	RORR (-)	

↑↓ represent different indicators that increased or decreased compared to the control group, respectively; (-) represents no significant difference compared to the control group.

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